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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants: Emanuel Hanski, et al.
Serial No.: 10/525,178 Examiner: Not Yet Known
Filed : August 19, 2003 Art Unit: Not Yet Known
For : COMPOSITIONS AND METHODS FOR THE TREATMENT AND
PROPHYLAXIS OF INFECTIONS CAUSED BY GRAM POSITIVE
BACTERIA

1185 Avenue of the Americas
New York, New York 10036
November 17, 2006

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Applicants are filing this Supplemental Information Disclosure Statement to supplement the Information Disclosure Statement filed on March 27, 2006 in connection with the above-identified application.

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following references which are listed on the attached Form PTO-1449 (**Exhibit A**). Copies of references 14-68 are attached hereto as **Exhibits 1-55**, respectively.

1. U.S. Patent No. 4,064,236, issued December 20, 1977, to Dorn et al.;

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2. U.S. Patent No. 4,457,917, issued July 3, 1984, to Schaller nee Kornmayer et al.;
3. U.S. Patent No. 4,639,435, issued January 27, 1987, to Fujii et al.;
4. U.S. Patent No. 4,755,383, issued July 5, 1988, to Fujii et al.;
5. U.S. Patent No. 4,900,549, issued February 13, 1990, to De Vries et al.;
6. U.S. Patent No. 5,164,372, issued November 17, 1992, to Matsuo et al.;
7. U.S. Patent No. 5,298,246, issued March 29, 1994, to Yano et al.;
8. U.S. Patent No. 5,354,900, issued October 11, 1994, to Matsuo et al.;
9. U.S. Patent No. 5,418,219, issued May 23, 1995, to Ueda;
10. U.S. Patent No. 5,439,688, issued August 8, 1995, to Orsolini et al.;
11. U.S. Patent No. 5,554,378, issued September 10, 1996, to Uda et al.;

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Page 3

12. U.S. Patent No. 5,733,877, issued March 31, 1998, to Sato et al.;
13. U.S. Patent No. 5,736,519, issued April 7, 1998, to Deigin et al.;
14. Ashbaugh, C. D., et al. (1998) "Molecular Analysis of the Role of the Group A Streptococcal Cysteine Protease, Hyaluronic Acid Capsule, and M Protein in a Murine Model of Human Invasive Soft-Tissue Infection," *J. Clin. Invest.* 102: 550-560 (**Exhibit 1**);
15. Barker, F. G., et al. (1987) "Streptococcal Necrotising Fasciitis: Comparison Between Histological and Clinical Features," *J. Clin. Pathol.* 40: 335-341 (**Exhibit 2**);
16. Beall, B., et al. (1996) "Sequencing *emm*-Specific PCR Products for Routine and Accurate Typing of Group A Streptococci," *J. Clin. Microbiol.* 34: 953-958 (**Exhibit 3**);
17. Berge, A., et al. (1998) "Identification of an Insertion Sequence Located in a Region Encoding Virulence Factors of *Streptococcus pyogenes*," *Infect. Immun.* 66: 3449-3453 (**Exhibit 4**);
18. Bisno, A. L., et al. (1996) "Streptococcal Infections of Skin and Soft Tissues," *N. Engl. J. Med.* 334: 240-245 (**Exhibit 5**);

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19. Chatellier, S., et al. (2000) "Genetic Relatedness and Superantigen Expression in Group A Streptococcus Serotype M1 Isolates from Patients with Severe and Nonsevere Invasive Diseases," *Infect. Immun.* 68: 3523-3534 (**Exhibit 6**);
20. Chaussee, M. S., et al. (1996) "Genetic and Phenotypic Diversity among Isolates of Streptococcus Pyogenes from Invasive Infections," *J. Infect. Dis.* 173: 901-908 (Abstract) (**Exhibit 7**);
21. Chiang, L., et al. (1999) "In Vivo Genetic Analysis of Bacterial Virulence," *Annu. Rev. Microbiol.* 53: 129-154 (**Exhibit 8**);
22. Cleary, P. P., et al. (1992) "Clonal Basis for Resurgence of Serious Streptococcus Pyogenes Disease in the 1980s," *Lancet* 339: 518-521 (**Exhibit 9**);
23. Cockerill, F. R., et al. (1998) "Molecular, Serological, and Clinical Features of 16 Consecutive Cases of Invasive Streptococcal Disease," *Clin. Infect. Dis.* 26: 1448-1458 (**Exhibit 10**);
24. Davies, H. D., et al. (1996) "Invasive Group A Streptococcal Infections in Ontario, Canada," *N. Engl. J. Med.* 335: 547-554 (**Exhibit 11**);
25. De Saizieu, A., et al. (2000) "Microarray-Based Identification of a Novel *Streptococcus pneumoniae* Regulon

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Controlled by an Autoinduced Peptide," *J. Bacteriol.* 182:
4696-4703 (**Exhibit 12**);

26. Engleberg, N. C., et al. (2001) "Spontaneous Mutations in the CsrRS Two-Component Regulatory System of *Streptococcus pyogenes* Result in Enhanced Virulence in a Murine Model of Skin and Soft Tissue Infection," *J. Infect. Dis.* 183: 1043-1054 (**Exhibit 13**);
27. Facklam, R., et al. (1999) "emm Typing and Validation of Provisional M Types for Group A Streptococci," *Emerg. Infect. Dis.* 5: 247-253 (**Exhibit 14**);
28. Ferretti, J. J., et al. (2001) "Complete Genome Sequence of an M1 Strain of *Streptococcus pyogenes*," *Proc. Natl. Acad. Sci. U.S.A.* 98: 4658-4663 (**Exhibit 15**);
29. Gresham, H. D., et al. (2000) "Survival of *Staphylococcus aureus* Inside Neutrophils Contributes to Infection," *J. Immunol.* 164: 3713-3722 (**Exhibit 16**);
30. Gryllos, I., et al. (2001) "Regulation of Capsule Gene Expression by Group A *Streptococcus* during Pharyngeal Colonization and Invasive Infection," *Mol. Microbiol.* 42: 61-74 (**Exhibit 17**);
31. Håvarstein, L. S., et al. (1997) "Natural Competence in the Genus *Streptococcus*: Evidence that Streptococci Can Change

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- Pherotype by Interspecies Recombinational Exchanges," *J. Bacteriol.* 179: 6589-6594 (**Exhibit 18**);
32. Havarstein, L. S., et al. (1995) "A Family of Bacteriocin ABC Transporters Carry Out Proteolytic Processing of their Substrates Concomitant with Export," *Mol. Microbiol.* 16: 229-240 (Abstract) (**Exhibit 19**);
33. Hensel, M., et al. (1995) "Simultaneous Identification of Bacterial Virulence Genes by Negative Selection," *Science* 269: 400-403 (Abstract) (**Exhibit 20**);
34. Hidalgo-Grass, C., et al. (2002) "A Locus of Group A Streptococcus Involved in Invasive Disease and DNA Transfer," *Mol. Microbiol.* 46: 87-99 (**Exhibit 21**);
35. Hui, F. M., et al. (1995) "Competence for Genetic Transformation in *Streptococcus pneumoniae*: Organization of a Regulatory Locus with Homology to Two Lactococcal A Secretion Genes," *Gene* 153: 25-31 (**Exhibit 22**);
36. Ji, Y., et al. (1996) "C5a Peptidase Alters Clearance and Trafficking of Group A Streptococci by Infected Mice," *Infect. Immun.* 64: 503-510 (**Exhibit 23**);
37. Kansal, R. G., et al. (2003) "Selective Modulation of Superantigen-Induced Responses by Streptococcal Cysteine Protease," *J. Infect. Dis.* 187: 398-407 (**Exhibit 24**);

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38. Kotb, M., et al. (2002) "An Immunogenetic and Molecular Basis for Differences in Outcomes of Invasive Group A Streptococcal Infections," *Nat. Med.* 8: 1398-1404 (**Exhibit 25**);
39. Kuo, C., et al. (1998) "Role of Streptococcal Pyrogenic Exotoxin B in the Mouse Model of Group A Streptococcal Infection," *Infect. Immun.* 66: 3931-3935 (**Exhibit 26**);
40. Lacks, S. A., et al. (2001) "Constitutive Competence for Genetic Transformation in *Streptococcus pneumoniae* Caused by Mutation of a Transmembrane Histidine Kinase," *Mol. Microbiol.* 42: 1035-1045 (**Exhibit 27**);
41. Lancefield, R. C., et al. (1957) "Differentiation of Group A Streptococci with a Common R Antigen into Three Serological Types, with Special Reference to the Bactericidal Test," *J. Exp. Med.* 106: 525-544 (**Exhibit 28**);
42. Lukomski, S., et al. (1999) "Extracellular Cysteine Protease Produced by *Streptococcus pyogenes* Participates in the Pathogenesis of Invasive Skin Infection and Dissemination in Mice," *Infect. Immun.* 67: 1779-1788 (**Exhibit 29**);
43. Lukomski, S., et al. (1997) "Inactivation of *Streptococcus pyogenes* Extracellular Cysteine Protease Significantly Decreases Mouse Lethality of Serotype M3 and M49 Strains," *J. Clin. Invest.* 99: 2574-2580 (**Exhibit 30**);

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44. Luster, A. D. (1998) "Chemokines - Chemotactic Cytokines that Mediate Inflammation," *N. Engl. J. Med.* 338: 436-445 (Exhibit 31);
45. Lyon, W. R., et al. (1998) "A Role for Trigger Factor and an Rgg-Like Regulator in the Transcription, Secretion and Processing of the Cysteine Proteinase of *Streptococcus pyogenes*," *Embo J.* 17: 6263-6275 (Exhibit 32);
46. Mecsas, J. (2002) "Use of Signature-tagged Mutagenesis in pathogenesis Studies," *Curr. Opin. Microbiol.* 5: 33-37 (Exhibit 33);
47. Medina, E., et al. (2003) "Survival of *Streptococcus pyogenes* within Host Phagocytic Cells: A Pathogenic Mechanism for Persistence and Systemic Invasion," *J. Infect. Dis.* 187: 597-603 (Exhibit 34);
48. Merrifield, B. (1986) "Solid Phase Synthesis," *Science* 232: 341-347 (Exhibit 35);
49. Miller, M. B., et al. (2001) "Quorum Sensing in Bacteria," *Annu. Rev. Microbiol.* 55: 165-199 (Exhibit 36);
50. Morrison, D. A., et al. (2000) "Regulation of Competence for Genetic Transformation in *Streptococcus pneumoniae*: A Link between Quorum Sensing and DNA Processing Genes," *Res. Microbiol.* 151: 445-451 (Exhibit 37);

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51. Moses, A. E., et al. (2002) "Invasive Group A Streptococcal Infections, Israel," *Emerg. Infect. Dis.* 8: 421-426 (**Exhibit 38**);
52. Moses, A. E., et al. (1997) "Relative Contributions of Hyaluronic Acid Capsule and M Protein to Virulence in a Mucoid Strain of the Group A *Streptococcus*," *Infect. Immun.* 65: 64-71 (**Exhibit 39**);
53. Moses, A. E., et al. (2003) "emm Typing of M Nontypeable Invasive Group A Streptococcal Isolates in Israel," *J. Clin. Microbiol.* 41: 4655-4659 (**Exhibit 40**);
54. Muotiala, A., et al. (1997) "Molecular Comparison of Group A Streptococci of T1M1 Serotype From Invasive and Noninvasive Infections in Finland," *J. Infect. Dis.* 175: 392-399 (Abstract) (**Exhibit 41**);
55. Norgren, M., et al. (1992) "Genetic Diversity in T1m1 Group A Streptococci in Relation to Clinical Outcome of Infection," *J. Infect. Dis.* 166: 1014-1020 (Abstract) (**Exhibit 42**);
56. Norrby-Teglund, A., et al. (2001) "Evidence for Superantigen Involvement in Severe Group A Streptococcal Tissue Infections," *J. Infect. Dis.* 184: 853-860 (**Exhibit 43**);

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57. O'Brien, K. L., et al. (2002) "Epidemiology of Invasive Group A Streptococcus Disease in the United States, 1995-1999," *Clin. Infect. Dis.* 35: 268-276 (**Exhibit 44**);
58. Pozzi, G., et al. (1996) "Competence for Genetic Transformation in Encapsulated Strains of *Streptococcus pneumoniae*: Two Allelic Variants of the Peptide Pheromone," *J. Bacteriol.* 178: 6087-6090 (**Exhibit 45**);
59. Ravins, M., et al. (2000) "Characterization of a Mouse-Passaged, Highly Encapsulated Variant of Group A Streptococcus in In Vitro and In Vivo Studies," *J. Infect. Dis.* 182: 1702-1711 (**Exhibit 46**);
60. Sherman, D. B., et al. (1990) "Compatibility of Thioamides with Reverse Turn Features: Synthesis and Conformational Analysis of Two Model Cyclic Pseudopeptides Containing Thioamides as Backbone Modifications," *J. Am. Chem. Soc.* 112: 433-441 (**Exhibit 47**);
61. Smoot, J. C., et al. (2002) "Genome Sequence and Comparative Microarray Analysis of Serotype M18 Group A *Streptococcus* Strains Associated with Acute Rheumatic Fever Outbreaks," *Proc. Natl. Acad. Sci. U.S.A.* 99: 4668-4673 (**Exhibit 48**);
62. Stanley, J., et al. (1995) "Molecular Subtyping of Prevalent M Serotypes of *Streptococcus pyogenes* Causing Invasive Disease," *J. Clin. Microbiol.* 33: 2850-2855 (**Exhibit 49**);

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63. Taylor, F. B., et al. (1999) "Staging of the Baboon Response to Group A Streptococci Administered Intramuscularly: A Descriptive Study of the Clinical Symptoms and Clinical Chemical Response Patterns," *Clin. Infect. Dis.* 29: 167-177 (**Exhibit 50**);
64. Thorsett, E. D., et al. (1983) "Dipeptide mimics. Conformationally Restricted Inhibitors of Angiotensin-converting Enzyme," *Biochem. Biophys. Res. Commun.* 111: 166-171 (Abstract) (**Exhibit 51**);
65. Van Damme, J., et al. (1997) "Granulocyte Chemotactic Protein-2 and Related CXC Chemokines: From Gene Regulation to Receptor Usage," *J. Leukoc. Biol.* 62: 563-569 (**Exhibit 52**);
66. Veber, D. F., et al. (1978) "Conformationally Restricted Bicyclic Analogs of Somatostatin," *Proc. Natl. Acad. Sci. U.S.A.* 75: 2636-2640 (**Exhibit 53**);
67. von Pawel-Rammingen, U., et al. (2003) "IdeS and SpeB: Immunoglobulin-Degrading Cysteine Proteinases of *Streptococcus pyogenes*," *Curr. Opin. Microbiol.* 6: 50-55 (**Exhibit 54**); and
68. Wexler, D. E., et al. (1985) "Mechanism of Action of the Group A Streptococcal C5a Inactivator," *Proc. Natl. Acad. Sci. U.S.A.* 82: 8144-8148 (**Exhibit 55**).

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Page 12

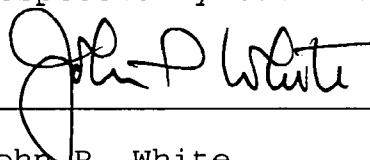
Applicants note that above-identified references 1-13 are issued U.S. patents. Accordingly, pursuant to 37 C.F.R. §1.98(a)(2)(ii), copies of these patents are not required to be provided to the United States Patent and Trademark Office.

Applicants request that the Examiner review the references listed above and make them of record in the subject application.

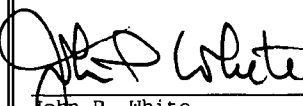
If a telephone interview would be of assistance in advancing prosecution of the subject application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

Pursuant to 37 C.F.R. §1.97(b)(3), no fee is deemed necessary in connection with the filing of this Supplemental Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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Registration No. 28,678
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I hereby certify that this correspondence is being deposited this date with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Arlington, VA 22313-1450	
 11/17/06	Date
John P. White Reg. No. 28,678	

Form PTO-1449 U.S. Department of Commerce Patent and Trademark Office INFORMATION DISCLOSURE STATEMENT (Use several sheets if necessary)	Application Number	10/525,178
	Filing Date	August 19, 2003
	First Named Inventor	Emanuel Hanski, et al.
	Art Unit	Not Yet Known
	Examiner Name	Not Yet Known
	Attorney Docket No.	1567/73975/JPW/MVM

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Document Number Number-Kind Code ² (if known)	Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document
	1	US 4,064,236	12-20-1977	Dorn et al.
	2	US 4,457,917	07-03-1984	Schaller nee Kornmayer et al.
	3	US 4,639,435	01-27-1987	Fujii et al.
	4	US 4,755,383	07-05-1988	Fujii et al.
	5	US 4,900,549	02-13-1990	De Vries et al.
	6	US 5,164,372	11-17-1992	Matsuo et al.
	7	US 5,298,246	03-29-1994	Yano et al.
	8	US 5,354,900	10-11-1994	Matsuo et al.
	9	US 5,418,219	05-23-1995	Ueda
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	12	US 5,733,877	03-31-1998	Sato et al.
	13	US 5,736,519	04-07-1998	Deigin et al.

FOREIGN PATENT DOCUMENTS

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Applicants: Emanuel Hanski, et al.

U.S. Serial No.: 10/525,178

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Exhibit A

ALL REFERENCES CONSIDERED EXCEPT WHERE LINED THROUGH. /MN/

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INFORMATION DISCLOSURE CITATION
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Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	14	Ashbaugh C. D., et al. (1998) "Molecular Analysis of the Role of the Group A Streptococcal Cysteine Protease, Hyaluronic Acid Capsule, and M Protein in a Murine Model of Human Invasive Soft-Tissue Infection," <i>J. Clin. Invest.</i> 102: 550-560	
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	17	Berge, A., et al. (1998) "Identification of an Insertion Sequence Located in a Region Encoding Virulence Factors of <i>Streptococcus pyogenes</i> ," <i>Infect. Immun.</i> 66: 3449-3453	
	18	Bisno, A. L., et al. (1996) "Streptococcal Infections of Skin and Soft Tissues," <i>N. Engl. J. Med.</i> 334: 240-245	
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				Art Unit	Not Yet Known
				Examiner Name	Not Yet Known
				Attorney Docket No.	1567/73975/JPW/MVM
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